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TITLE: Trimodel Mammography with Perfect Coregistration

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RECIPIENT: University of Wisconsin System
Madison, WI 53715-1218

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University of Wisconsin System
Madison, WI 53715-1218

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14. ABSTRACT
This project aims at developing a trimodel x-ray mammography imaging system to improve both sensitivity and specificity in breast cancer screening and diagnosis, particularly for radiologically dense breasts. In the proposed system, three complementary image datasets will be generated from a single data acquisition: the first is the conventional absorption contrast mammography image, the second is a novel phase contrast mammography image with enhanced edges and reduced anatomical background, the major confounding factor in reading mammography; the imaging characteristics suggest that this contrast mechanism would be preferable for cancer mass detection. The third image is the dark-field mammogram, which is sensitive to the local distribution of microcalcifications, calcified vessels, and other small objects in the breast. The proposed system will be constructed, optimized, and evaluated using mastectomy specimens.

15. SUBJECT TERMS-

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1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

This project aims at developing a trimodel x-ray mammography imaging system to improve both sensitivity and specificity in breast cancer screening and diagnosis, particularly for radiologically dense breasts. In the proposed system, three complementary image datasets will be generated from a single data acquisition: the first is the conventional absorption contrast mammography image, the second is a novel phase contrast mammography image with enhanced edges and reduced anatomical background, the major confounding factor in reading mammography; the imaging characteristics suggest that this contrast mechanism would be preferable for cancer mass detection. The third image is the dark-field mammogram, which is sensitive to the local distribution of microcalcifications, calcified vessels, and other small objects in the breast. The proposed system will be constructed, optimized, and evaluated using mastectomy specimens.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

Early breast cancer detection, dense breast, mammography, x-ray phase contrast imaging, x-ray dark field imaging, Talbot-Lau interferometer

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

As stated in the approved SOW, the major goals of the project include:

1. Develop a grating interferometer for a trimodal mammography system
2. Integrate the grating interferometer into existing digital mammography system
3. Objective and quantitative performance evaluation of the proposed system
4. Subjective performance evaluation of the proposed system using mastectomy specimens

Specific tasks for this reporting period (01/15/2015-01/14-2017) include:

1. Develop system modeling tool (completed in 04/2016)
2. Optimize the analyzer grating design (completed in 05/2016)
3. Optimize the design of other interferometer components (completed in 06/2016)
4. Grating fabrication (completed in 07/2016)
5. Modify the current x-ray breast imaging system (completed in 12/2016)
6. Calibrate the interferometer and detector responses (percentage of completion: 50%)
7. Physical performance assessments (50%)
8. Human subject regulatory review and approval by the USAMRMC HRPO and local IRB (completed in 10/2016)

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

A. Major activities

During this reporting period (01/15/2015-01/14-2017), the following major activities were performed:

1. Design, optimization, and fabrication of a grating interferometer system for the proposed trimodal mammography imaging system
2. Characterization of the grating interferometer system
3. Construction of the trimodal mammography imaging system by integrating the grating interferometer with a conventional mammography system
4. Objective characterization of the constructed trimodal mammography imaging system
5. Disseminate research findings through conference presentations and journal publications

B. Specific objectives

The major objective of Year 1 is to construct a trimodel mammography imaging system and get it ready for the proposed mastectomy specimen studies.

C. Key outcomes

C.1 Design of Talbot-Lau grating interferometer

- Major finding: Major parameters of these gratings, including their pitch, duty cycle, aspect ratio, and material, have been determined and are listed in Table I. For the G2 grating, it contains a staircase structure shown in Figure 1: the grating lines are shifted by 0.551 μm for every 70 μm.

Table I Grating Parameters

Grating	Wafer size	Effective area	Pitch	Duty cycle	Material of x-ray absorber	Depth of x-ray absorber
G0	4 inch	3×3 cm^2	22.96 μm	58%	Gold	100 μm
G1	6 inch	7×7 cm^2	4 μm	50%	Nickle	11 μm
G2	4 inch	5×5 cm^2	2.19 μm	50%	Gold	50 μm

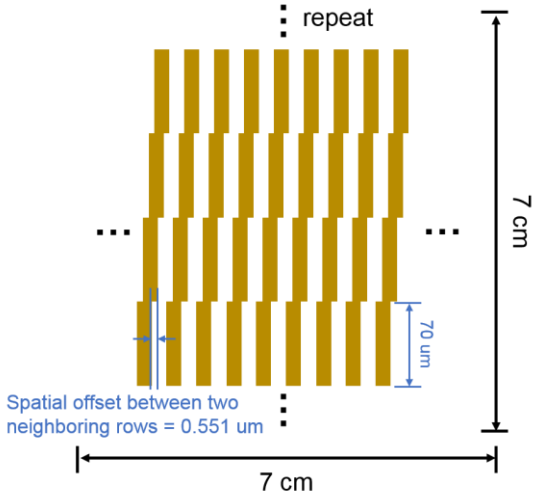

Figure 1 Staggered design for the G2 grating

C.2 Results of grating fabrication and characterization

Based on the design given in C.1, a set of three gratings (G0, G1, and G2) was successfully fabricated.

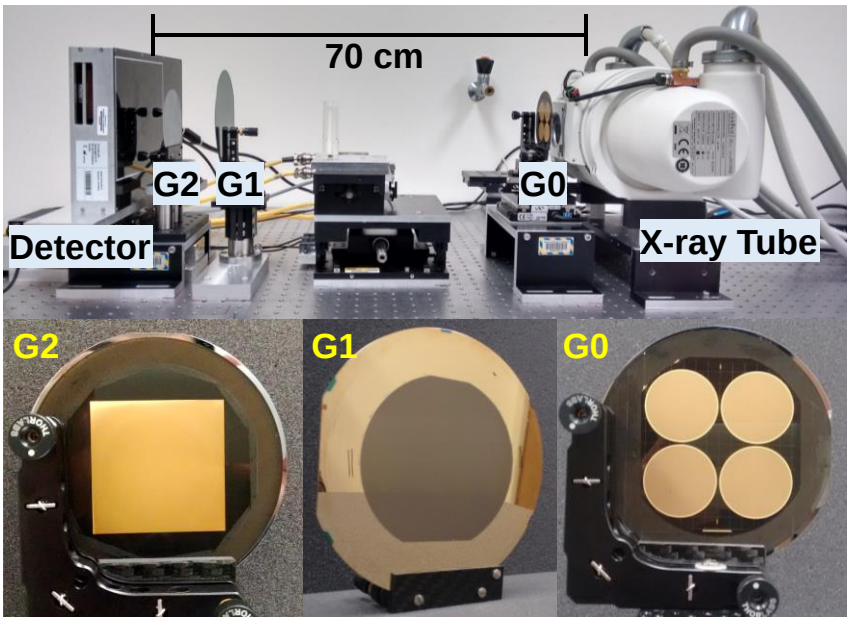

Figure 2 Trimodal benchtop imaging system with three gratings.

Performance of the gratings was tested in a benchtop imaging environment shown in Figure 2. The uniformities of the fabricated gratings were characterized by taking their x-ray projection images and measuring the relative variation of the image signal value across different ROIs. As shown in Figure 3, the relative variabilities for G0, G1, and G2 are 0.6%, 0.2%, and 5%, respectively.

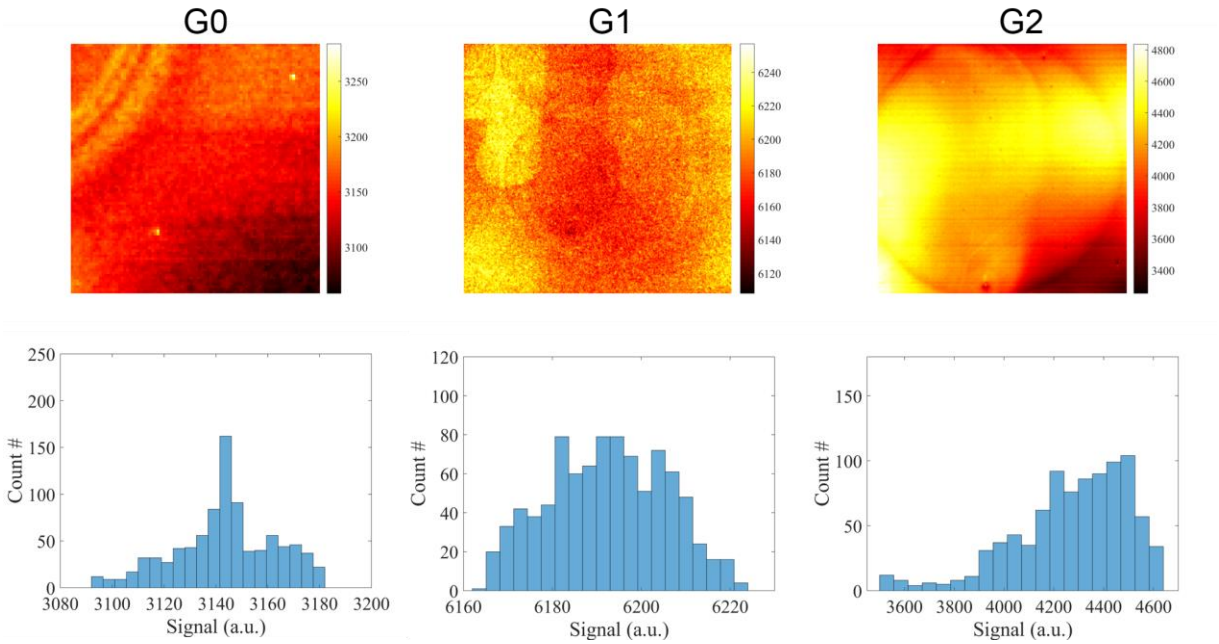

Figure 3 Top row: x-ray projection images of the three gratings. Bottom row: Uniformity of the gratings characterized by the histograms of the mean signal values measured in different ROIs in the gratings.

Wave optical performance of the Talbot-Lau interferometer constructed from the three fabricated gratings was characterized by the fringe visibility. As shown by the fringe visibility map in Figure 2, the average fringe visibility is 15%±3%.

- Major finding: Talbot-Lau interferometer designed for compact mammography geometry is achievable with decent uniformity and fringe visibility.

C.3 Results of system modification

To construct the proposed trimodal mammography imaging system, a conventional x-ray digital mammography system (Figure 4) was modified.

Figure 4 A full field digital mammography system (Senographe 2000 D, GE Healthcare) in the PI's lab was used to construct the trimoal mammography imaging system.

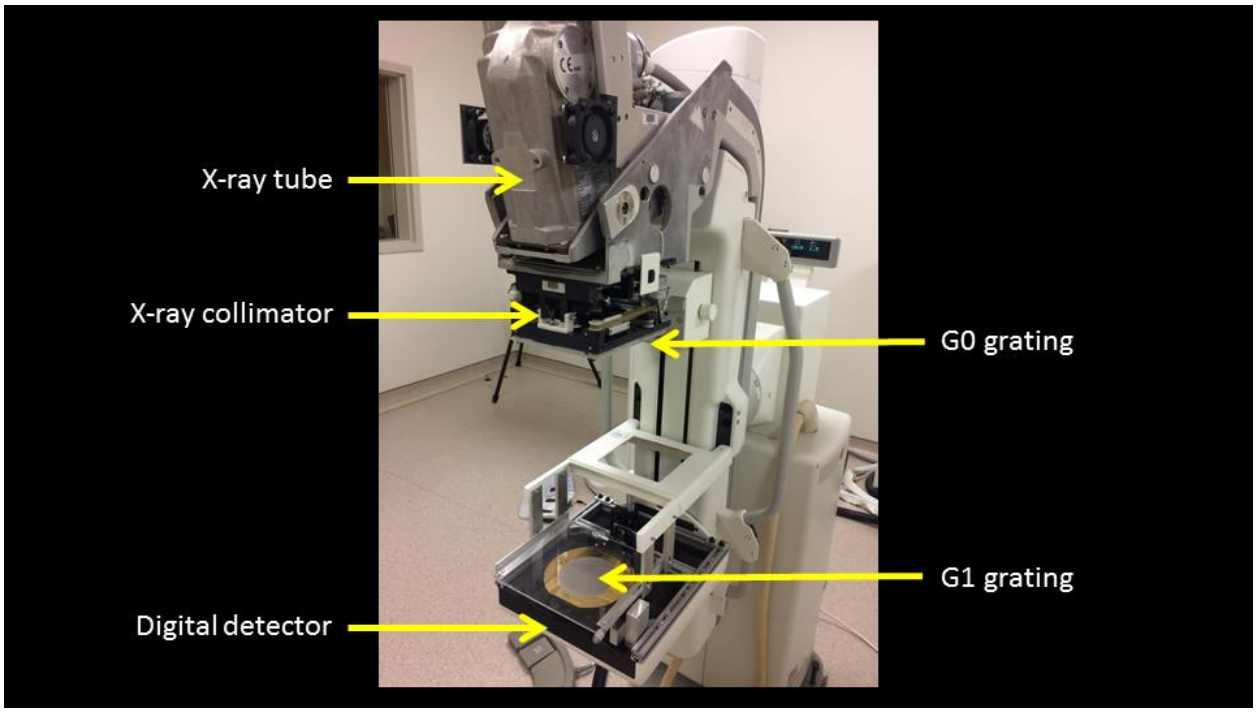

Figure 5 Modified mammography imaging system. Close-ups of the fixtures for the gratings are provided in Figure 6.

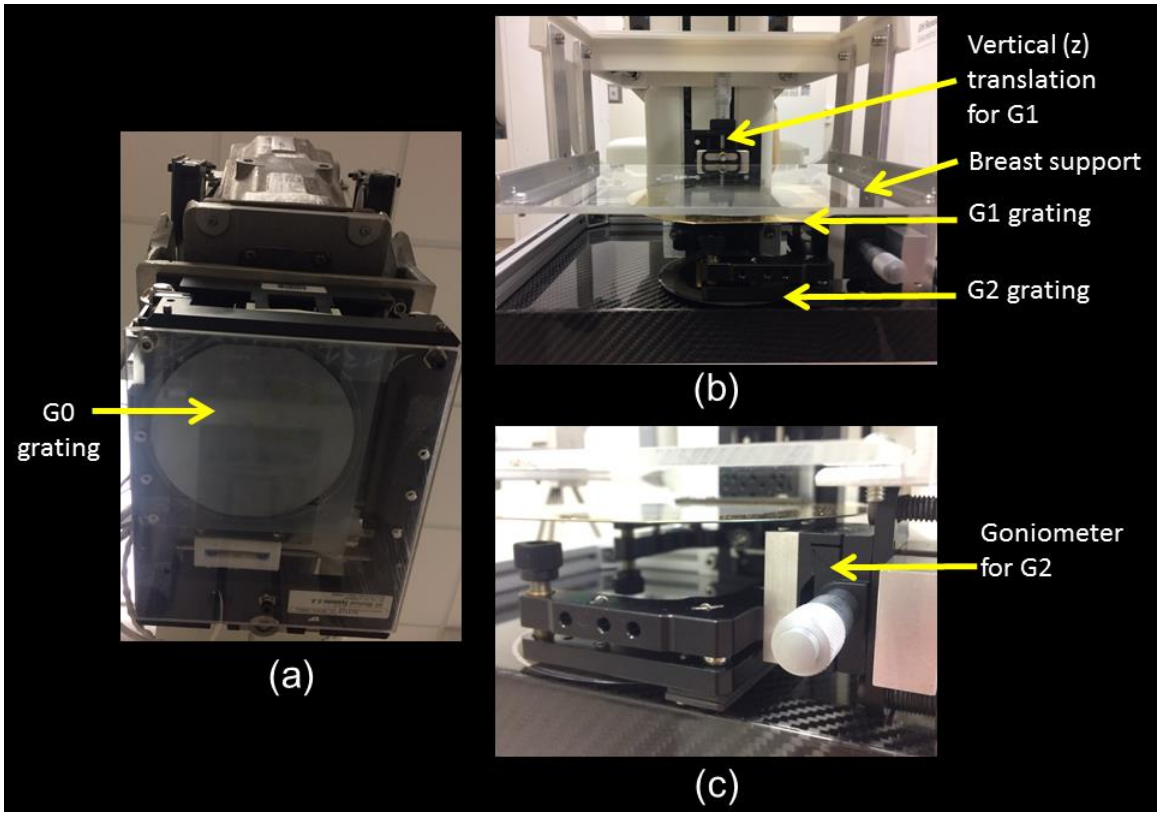

Figure 6 (a) The source grating G0 was attached to the exit window of the x-ray collimator assembly. (b) The phase grating G1 and analyzer grating G2 were installed above the detector surface. (c) A close-up of the optical system.

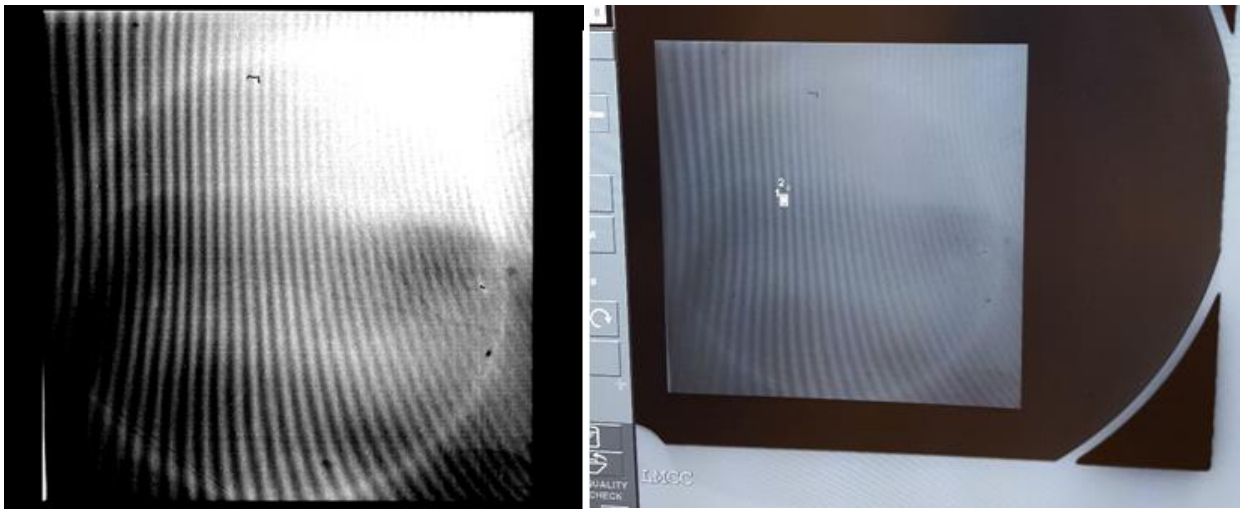

Figure 7 Moiré pattern generated by the constructed trimodal mammography imaging system.

Figure 5 shows the modified system, and Figure 6 demonstrates how the three gratings were incorporated into the existing mammography system. The source grating G0 was directly attached to the exit window of the x-ray collimator assembly. No other optical device was used for this grating. The phase grating G1 was installed to an optics mount, which was then attached to a goniometer and a vertical translation stage. The optics mount and the goniometer allow the angular position (pitch, yaw, roll) of G1 to be adjusted, while the translation stage helps to adjustment the relative distance between G1 and G2. The analyzer grating was fixed in a position that is directly above the detector surface. An optics mount and a goniometer provide the needed degrees of freedom in aligning its angular position relative to G0.

To align the three gratings, orientation of grating structure in G0 was used as a reference, and both G1 and G2 were adjusted to align with G0. After collinearity of the three gratings was established, the vertical position of G1 was adjusted to fine-tune the visibility of the moiré pattern. Figure 7 shows a moiré pattern generated by the modified system, indicating success in generating the x-ray diffraction.

- Major finding: Trimodal x-ray mammography imaging is achievable by combining Talbot-Lau interferometer with a conventional mammography system. No modification to the x-ray tube or detector is required, as all three gratings can be placed outside the tube/detector housing.

C.4 Radition reduction for trimodal mammography using a photon counting detector

Based on the low dimensionality of the phase contrast images generated from different energy bins of an energy-resolving photon counting detector (PCD), we have developed a method to reduce noise of phase contrast images (Optics Express, 24, pp.12955, 2016). Figure 8 compares phase contrast images generated with or without the proposed method. This method can potentially be used to improve the radiation dose efficiency of the proposed trimodal mammography imaging system.

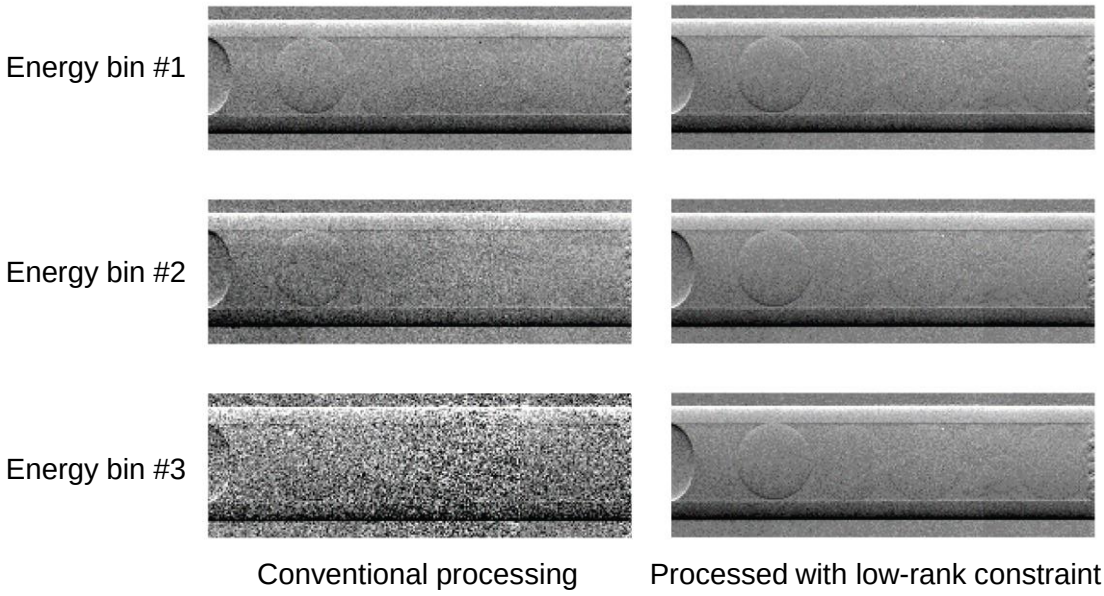

Figure 8 Phase contrast images of a physical phantom. Images in the left row were generated from the three energy bins of the PCD with standard processing. Images in the right row were processed using the proposed rank-one approximation method (adapted from *Optics Express*, Vol. 24, pp.12955, 2016).

- Major finding: The energy resolving capability of PCD can be used to further reduce radiation dose in x-ray phase contrast imaging.

C.5 Investigation of signal bias in trimodal mammography

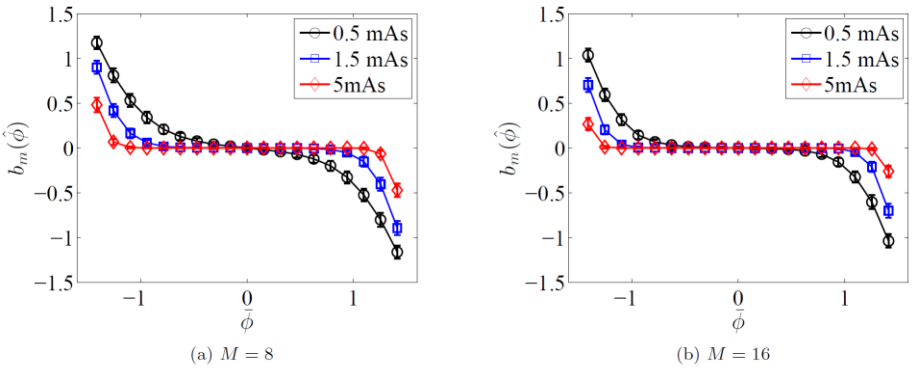

Figure 9: Dependence of the measured bias of ϕ [denoted as $b_m(\phi)$] on ϕ for different total number of phase steps (M) and mAs.

- Major finding: the bias for absorption contrast signal is zero, and the signal bias for dark field contrast is inversely proportional to the number of phase steps and to the average fringe visibility of the grating interferometer. The bias of phase contrast signal (denoted as ϕ) is related to the expected value of ϕ, the exposure level, and the interferometer performance (Figure 9).

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

The University of Wisconsin-Madison requires that all graduate students and postdoctoral researchers supported by federal funding utilize Individual Development Plans to set academic and career goals and facilitate conversations with their mentors. The university offers a collection of resources and tools to support mentees, mentors, and PIs in implementing IDPs. These include a UW-Madison IDP template, workshops for mentees (both face-to-face and online videos), peer learning groups for mentees, as well as guidelines for mentors.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

We published results in peer reviewed journals such as Optics Express and conference proceedings such as Proceeding of SPIE. The results were also disseminated to the breast imaging research community via our presentations at medical imaging conferences such as RSNA.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

During the next reporting period (01/15/2017-01/14/2018), we plan to perform the following research activities:

1) Characterize the physical performance of the modified system
We will assess the physical performance the modified system using both zero frequency and frequency dependent metrics. We will also measure the mean glandular dose of the modified system for each kV and mAs combination, as the incorporation of the gratings into the x-ray beam may alter the beam quality. Results of the performance characterization will be used to guide the optimization of trimodal mammography image acquisition protocol.

2) Task-driven image acquisition protocol optimization
The purpose of this task is to find the optimal multi-contrast image acquisition parameters (e.g., tube current, x-ray pulse time, and tube potential). Breast anatomical noise in the acquired multi-contrast mammographic images will be characterized and used to calculate generalized model observer detectability index for both mass detection and calcification detection tasks. The generalized detectability index will be used as the figure-of-merit to guide the optimization of image acquisition parameters.

3) Collection of mastectomy specimens and perform trimodal mammographic image acquisitions
Under a human subject research protocol proved by the IRB and HRPO, fresh mastectomy specimens will be transferred directly from the operating room to the trimodal mammography suite, where multi-contrast images will be acquired using the optimized protocol. After the image acquisition, the specimens will be transferred to pathology lab for histology studies.

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Research development in Year 1 is likely to make direct impact on the translation of the x-ray phase contrast imaging technology to clinical mammography, as it demonstrated how to design gratings for the geometry and x-ray spectrum of clinical mammography system. It also provides

technical details on how to modify a conventional mammography to enable three x-ray contrast mechanisms to be generated from the same data acquisition. The field of x-ray phase contrast and dark field imaging would potentially benefit from the research development, which for the first time demonstrated the feasibility of x-ray multi-contrast imaging using a clinical full field digital mammography system.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report.

5. CHANGES/PROBLEMS: The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to Report.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

During the third quarter of Year 1, the mammography imaging system encountered an unexpected collimator error that prohibited any x-ray exposure to be taken. This problem was reported in the quarterly report. In November 2016, replacement of the failed collimator assembly was done, and the error was successfully resolved. The grant officer was notified immediately on December 1st, 2016. As of today, delays caused by this unexpected system error have largely been mitigated.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

One of the co-investigators, Dr. DeMartini, has left the University of Wisconsin for another job position at Stanford University. We are currently in the process of identifying a breast radiologist at our institution to replace Dr. DeMartini's role (1.2 calendar months starting from Year 2) in this DOD project. Once the candidate is identified, we will apply for approval from the grant officer.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals.

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  1. Y. Ge, R. Zhang, K. Li, G.-H. Chen, "Improving radiation dose efficiency of X-ray differential phase contrast imaging using an energy-resolving grating interferometer and a novel rank constraint." Optics Express, Vol. 24, Issue 12, page 12955-12968 (2016) http://dx.doi.org/10.1364/OE.24.012955
  2. X. Ji, Y. Ge, R. Zhang, K. Li, G.-H. Chen, "Studies of signal estimation bias in grating-based x-ray multi-contrast imaging." Medical Physics (accepted)

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report.

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Conference papers

1. Y. Ge, R. Zhang, K. Li, G.-H. Chen, "X-ray differential phase contrast imaging using a grating interferometer and a single photon counting detector," Proc. SPIE, 9783, 97830M (2016) http://dx.doi.org/10.1117/12.2216321
2. R. Zhang, B. Qin, Y. Ge, B. Whiting, K. Li, F. Villanueva, G.-H. Chen, "Potential use of micorobubles (MBs) as contrast material in x-ray dark field (DF) imaging: How does the DF signal change with the characteristic parameters of the MBs?," Proc. SPIE, 9783, 97830N (2016) http://dx.doi.org/10.1117/12.2216322

Conference presentations

1. X. Ji, Y. Ge, R. Zhang, K. Li, G.-H. Chen, "Low Dose Performance of a CdTe Single Photon Counting Detector and Its Application in Radiation Dose Reduction for X-ray Differential Phase Contrast Imaging." Radiological Society of North America 2016 Scientific Assembly and Annual Meeting, November 27 - December 2, 2016, Chicago IL. http://archive.rsna.org/2016/16014702.html (RSNA Student Travel Stipend Award)
2. Y. Ge, X. Ji, R. Zhang, K. Li, G.-H. Chen, "Radiation Dose Reduction in X-ray Differential Phase Contrast Breast Imaging using an Energy-resolved Grating Interferometer." Radiological Society of North America 2016 Scientific Assembly and Annual Meeting, November 27 - December 2, 2016, Chicago IL. htt://archive.rsna.org/2016/16015423.html

- **Website(s) or other Internet site(s)**
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report.

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

Nothing to Report.

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report.

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *biospecimen collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?
Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."

Example:

Name:	*Mary Smith*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	*1234567*
Nearest person month worked:	*5*
Contribution to Project:	*Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support:	*The Ford Foundation (Complete only if the funding support is provided from other than this award).*

Name: *Ke Li*
Project Role: *PI*
Nearest person month worked: *3*
Contribution to Project: *Dr. Li has performed work in the design and characterization of the grating interferometer, construction of the trimodal mammography imaging system, system alignment and assessment.*

Name: *Guang-Hong Chen*
Project Role: *Co-Investigator*
Nearest person month worked: *2*
Contribution to Project: *Dr. Chen has performed work in the wave optics modeling of the Talbot-Lau interferometer, design and optimization of the gratings*

Name: *Yongshuai Ge*
Project Role: *Graduate Student*
Nearest person month worked: *9*
Contribution to Project: *Mr. Ge has performed work in the design and characterization of the grating interferometer. He has also developed a method to improve the radiation dose efficiency of the proposed trimodal mammography imaging system using photon counting detector and a novel low-rank constraint.*

Name: *Xu Ji*
Project Role: *Graduate Student*
Nearest person month worked: *9*
Contribution to Project: *Mr. Ji has performed work in the design, modification and characterization of an x-ray mammography imaging system. He has also investigated the potential bias in the multi-contrast image signal.*

Name: *Ran Zhang*
Project Role: *Post-doc Associate/Assistant Scientist*
Nearest person month worked: *6*
Contribution to Project: *Dr. Zhang has performed work in the wave-optical modeling of the grating interferometer system and the fundamental physics for dark field imaging. He has also worked on the design of the grating interferometer and the construction of the trimodal mammography imaging system.*

Name: *Amy Fowler*
Project Role: *Co-Investigator*
Nearest person month worked: *1*
Contribution to Project: *Dr. Fowler has performed work in the design and revision of the human use regulatory protocol.*
Funding Support: *UW-Madison ICTR KL2 Scholars Program*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what

has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

ACTIVE OTHER SUPPORT

Li, Ke

U01 EB021183 (Chen, GH)
Project title: One Stop Shop Imaging for Acute Ischemic Stroke Treatment
Funding agency: NIH/NIBIB
Project goal: Develop and validate revolutionary imaging technologies that will result in the availability of a new image guided workflow for the diagnosis, triage, and endovascular treatment of patients presenting with an acute ischemic stroke due to a large artery occlusion.
Start and end date: 9/30/2015-6/30/2019
Role: Co-investigator
Level of effort: 3.6 calendar months
Point of contact at the funding agency: SASTRE, ANTONIO sastrea@mail.nih.gov

R01 EB020521-01 (Chen, GH and Li, K)
Project title: Multi-Contrast X-Ray Breast Imaging
Funding agency: NIH/NIBIB
Project goal: Develop a phase contrast digital breast tomosynthesis system and evaluate its potential utility in improving the sensitivity and specificity of breast cancer diagnosis through pilot human subject studies.
Start and end date: 01/01/2016-12/31/2019
Role: co-PI
Level of effort: 5.4 calendar months
Point of contact at the funding agency: SHABESTARI, BEHROUZ shabestb@mail.nih.gov

Chen, Guang-Hong

R01 CA169331-02 (Chen, GH and Pickhardt, P)
Project title: Ultra-Low Radiation Dose Body CT Imaging
Funding agency: NIH/NCI
Project goal: The overarching objective of the proposal is to develop, optimize, and evaluate an iterative image reconstruction algorithm that holds a promise to reduce radiation dose level by 70%-90% without compromising diagnostic accuracy.
Start and end date: 08/08/2012-05/31/2017
Level of effort: 2.88 calendar months
Point of contact at the funding agency: HENDERSON, LORI A. hendersonlori@mail.nih.gov

U01 EB021183 (Chen, GH)
Project title: One Stop Shop Imaging for Acute Ischemic Stroke Treatment
Funding agency: NIH/NIBIB
Project goal: Develop and validate revolutionary imaging technologies that will result in the availability of a new image guided workflow for the diagnosis, triage, and endovascular treatment of patients presenting with an acute ischemic stroke due to a large artery occlusion.
Start and end date: 9/30/2015-6/30/2019
Role: PI
Level of effort: 3.84 calendar months
Point of contact at the funding agency: SASTRE, ANTONIO sastrea@mail.nih.gov

R01 EB020521-01 (Chen, GH and Li, K)
Project title: Multi-Contrast X-Ray Breast Imaging
Funding agency: NIH/NIBIB
Project goal: Develop a phase contrast digital breast tomosynthesis system and evaluate its potential utility in improving the sensitivity and specificity of breast cancer diagnosis through pilot human subject studies.
Start and end date: 01/01/2016-12/31/2019
Role: co-PI
Level of effort: 2.88 calendar months
Point of contact at the funding agency: SHABESTARI, BEHROUZ shabestb@mail.nih.gov

DeMartini, Wendy

Dr. DeMartini has left the University of Wisconsin for another job position at Stanford University. We are currently in the process of identifying the replacement for Dr. DeMartini's role in this DOD project.

Fowler, Amy

Research Seed Grant RSD1420 (PI: Fowler)
Project Title: Impact of Endocrine-resistant Estrogen Receptor-α Variants on [18F]Fluoroestradiol Imaging of Breast Cancer
Funding agency: RSNA
Project goal: The long term goal is to develop a better understanding of ERalpha-dependent factors influencing FES imaging of patients with advanced/metastatic breast cancer in situations of endocrine resistance and yield molecular evidence regarding the mechanisms of FES as a predictive imaging biomarker
Role: PI
Start and end date: 7/1/2014-6/30/2017
Level of effort: (1% no salary support)
Point of contact at the funding agency: WALTER, SCOTT A. SWALTER@RSNA.ORG

KL2TR000428 (PI: Drezner)
Project Title: [18F]FFNP-PET Imaging of Progesterone Receptor as a Biomarker of Endocrine Sensitivity in Patients with Breast Cancer
Funding agency: NIH/NCATS-Institutional Clinical and Translational Science (ICTR)
Project goal: Goal is to test 1) the precision and accuracy of quantitative FFNP-PET imaging and 2) whether it can distinguish endocrine-sensitive from endocrine-resistant ERα+PR+ breast cancers.
Role: KL2 Scholar
Start and end date: 01/01/2016-present
Level of effort: 9 calendar months
Point of contact at the funding agency: Peggy Hatfield pmhatfie@wisc.edu

NOTE: In this DOD Breakthrough Award, Dr. Amy Fowler was listed as a co-investigator with an effort of 1.2 calendar months per year from Years 2 to 3. However, Dr. Fowler was selected to become one of the KL2 awardees at our institution (listed above). This award requires a 75% commitment of research time, and the goal of this award is to establish Dr. Fowler as a clinician-scientist, enabling the clinical translation of new technologies, such as that which will be developed in our project. Due to the scientific overlap between Dr. Folwer's proposed work on the DOD award and the career development goals defined in her KL2 award, her contribution to Dr. Li's DOD award is synergistic with her ICTR KL2 research project. Both investigators are studying novel imaging methods for improved detection and characterization of breast cancer. Furthermore, one of Dr. Fowler's career goals is to move breast imaging to both a more molecular and quantitative level.

Friedl, Andreas

UM1 CA186716-02 (Dipaola & Liu)
Project Title: Wisconsin and New Jersey Alliance in Precision Experimental Therapeutics
Funding agency: RBHS -CANCER INSTITUTE OF NEW JERSEY
Project goal: To merge two strong prior Phase I (U0l) sites to create the Wisconsin and New Jersey Alliance in Precision Experimental Therapeutics (WIN-Alliance). This group, as a synergistic, multidisciplinary and multi-institutional model, will develop and evaluate innovative, early phase experimental therapeutic clinical trials to improve clinical outcomes
Start and end date: 03/19/2014-02/28/2019
Role: Co-investigator
Level of effort:3%
Point of contact at the funding agency: Ivy, S. Percy ivyp@ctep.nci.nih.gov

VA Merit Review Program I01BX000137-07 (Friedl)
Project Title: Glypican-1 in Gliomagenesis
Funding agency: Department of Veterans Affairs
Project goal: This project focuses on studying the role of the heparin sulfate proteoglycan glypican-I in regulating the cell cycle in gliomas. The work is based on our observation that glypican-1 is overexpressed in the vast majority of glioma tumors and that overexpression of glypican-1 in glioma cells in vitro induces G1-S transition, DNA re- replication and DNA damage. We believe that glypican-1 overexpression in gliomas contributes to loss of growth control and genetic instability.
Start and end date: 04/01/2009-03/31/2017
Role: PI
Level of effort: 1.8 calendar months
Point of contact at the funding agency: Smith, Samantha Samantha.Smith10@va.gov

W81XWH-14-1-0274 (Friedl)
Project Title: Syndecan-1 and Metastasis Dormancy
Funding agency: DOD/Army
Project goal: This project aims at understanding the role of the heparan sulfate proteoglycan syndecan-1 in the escape of disseminated breast carcinoma cells from dormancy. Specifically, the goals are to 1) Determine the role of stromal syndecan-1 in escape of disseminated breast carcinoma cells from dormancy in vivo; 2) Determine the mechanism of disseminated breast carcinoma cell dormancy and metastatic outgrowth; and 3) Determine the cell type responsible for syndecan-1-dependent escape from dormancy
Start and end date: 08/01/2014-07/31/2017
Role: PI
Level of effort: 1.8 calendar months
Point of contact at the funding agency: Wendy A. Baker, grants officer wendy.a.baker.civ@mail.mil

U01 CA189283-01A1 (Seewaldt)
Project Title: Combined breast MRI/biomarker Strategies to Identify Aggressive Biology
Funding agency: NIH/NCI
Project goal: The goal of this research is to test from the bench to the clinic the hypothesis that loss of the tumor suppressor WWOX 1) in preclinical models mechanistically activates of glycolysis in metastatic TNBC via transcriptional activation HIF1α and 2) in primary and metastatic TNBC activates metabolism as measured by Fluorescence Lifetime Imaging (FLIM).
start and end date: 8/1/2015-7/31/2020
Role: Co-investigator
Level of effort: 0.3 calendar months
Point of contact at the funding agency: MAZURCHUK, RICHARD V mazurchukrv@mail.nih.gov

R01 EB020521-01 (Chen, GH and Li, K)
Project title: Multi-Contrast X-Ray Breast Imaging
Funding agency: NIH/NIBIB
Project goal: Develop a phase contrast digital breast tomosynthesis system and evaluate its potential utility in improving the sensitivity and specificity of breast cancer diagnosis through pilot human subject studies.
Start and end date: 01/01/2016-12/31/2019
Role: Co-investigator
Level of effort: 0.6 calendar months
Point of contact at the funding agency: SHABESTARI, BEHROUZ shabestb@mail.nih.gov

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have

provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.
Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to https://ers.amedd.army.mil for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.

9. APPENDICES: Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

No appendix to attach.